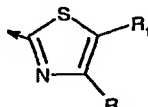


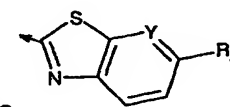
What is claimed is:

1. A compound of the formula

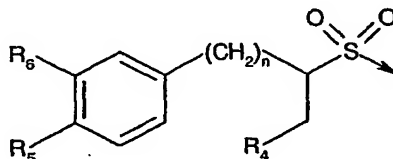


wherein

(i) Q is a  radical in which R<sub>1</sub> and R<sub>2</sub> are independently hydrogen or halogen;  
or

Q is a  radical in which R<sub>3</sub> is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl; Y is CH or nitrogen; and

R is a radical of the formula



wherein

R<sub>4</sub> is C<sub>2-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl or C<sub>5-7</sub>heterocycloalkyl;

R<sub>5</sub> and R<sub>6</sub> are independently hydrogen, halogen, cyano, R<sub>7</sub>, -C(O)R<sub>7</sub> or -S(O)<sub>2</sub>R<sub>7</sub>;

wherein

R<sub>7</sub> is -(CR<sub>8</sub>R<sub>9</sub>)<sub>m</sub>-W-R<sub>10</sub> in which

R<sub>8</sub> and R<sub>9</sub> are independently hydrogen or lower alkyl;

W is a bond, O, S or -NR<sub>11</sub> in which

R<sub>11</sub> is hydrogen or lower alkyl;

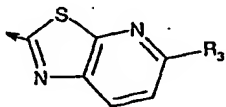
R<sub>10</sub> is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or R<sub>10</sub> and R<sub>11</sub>,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

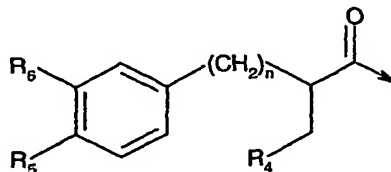
n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(ii) Q is a radical in which  $R_3$  is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl; and

R is a radical of the formula



wherein

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$  or  $-S(O)_2R_7$

wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are independently hydrogen or lower alkyl;

W is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

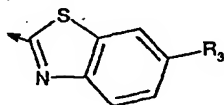
$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ ,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

m is zero or an integer from 1 to 5;

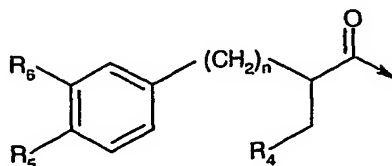
n is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(iii) Q is a radical in which  $R_3$  is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl; and

R is a radical of the formula



wherein

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$  or  $-S(O)_2R_7$

wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are independently hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ ,

combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

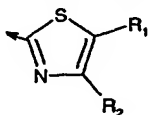
$m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

provided that: (1)  $R_5$  and  $R_6$  are not halogen when  $n$  is zero; or (2)  $R_5$  is not

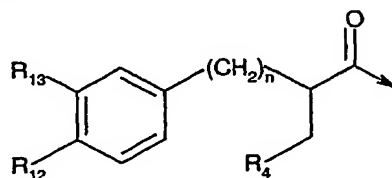
$-S(O)_2R_7$ , wherein  $R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which  $m$  is zero,  $W$  is a bond and  $R_{10}$  is  $C_{1-3}$ alkyl when  $n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof; or



(iv)  $Q$  is a radical, wherein  $R_1$  and  $R_2$  are independently hydrogen or halogen; and

$R$  is a radical of the formula



wherein

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_{12}$  and  $R_{13}$  are independently hydrogen, halogen, cyano,  $R_{14}$ ,  $-C(O)R_{14}$ , or  $-S(O)_2R_{14}$  wherein

$R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which

$R_8$  and  $R_9$  are independently hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{15}$  is cycloalkyl, aryl or heterocyclyl; or  $R_{15}$  and  $R_{11}$ , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

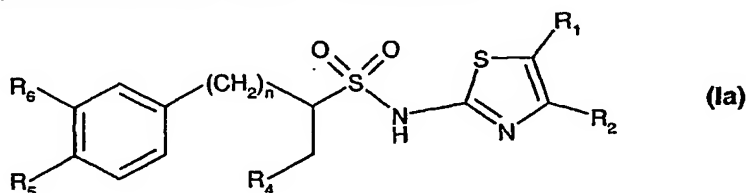
$m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

provided that: (1)  $R_{12}$  and  $R_{13}$  both are not hydrogen, halogen, cyano or combinations thereof; (2)  $R_{12}$  is not  $-S(O)_2R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is a bond when  $n$  is zero; (3)  $R_{12}$  is not  $-S(O)_2R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $R_8$  and  $R_9$  are hydrogen,  $m$  is 1 and  $W$  is a bond when  $n$  is zero; (4)  $R_{12}$  is not  $R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is O when  $n$  is zero; or (5)  $R_{12}$  is not  $R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is a bond when  $n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

2. A compound according to Claim 1 of the formula



wherein

$R_1$  and  $R_2$  are independently hydrogen or halogen;

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$  or  $-S(O)_2R_7$  wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are independently hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;  
 $m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

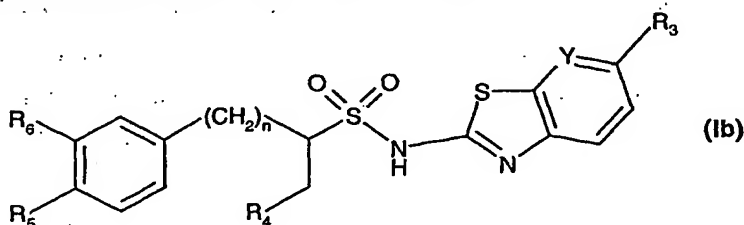
3. A compound according to Claim 2, wherein

$R_4$  is cyclopentyl;

$n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

4. A compound according to Claim 1 of the formula



wherein

$R_3$  is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl;

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$  or  $-S(O)_2R_7$  wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are, independently, hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which  $R_{11}$  is hydrogen or lower alkyl;

$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

$m$  is zero or an integer from 1 to 5;

$Y$  is CH or nitrogen;

$n$  is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

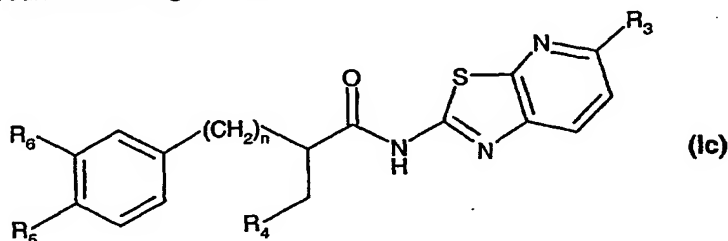
5. A compound according to Claim 4, wherein

$R_4$  is cyclopentyl;

$n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

6. A compound according to Claim 1 of the formula



wherein

$R_3$  is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl;

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$  or  $-S(O)_2R_7$  wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are, independently, hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

$m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

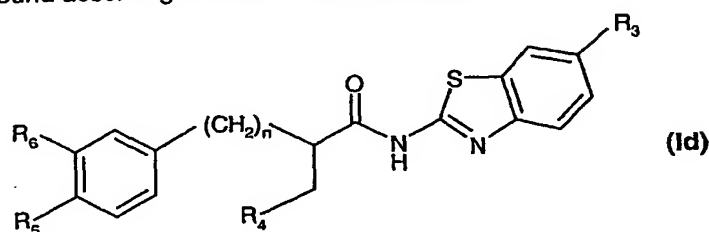
7. A compound according to Claim 6, wherein

$R_4$  is cyclopentyl;

$n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

8. A compound according to Claim 1 of the formula



wherein

$R_3$  is hydrogen, halogen, alkyl, cycloalkyl, aryl, alkoxy, cycloalkoxy, aryloxy, alkylthio, cycloalkylthio, arylthio, acyl, sulfonyl, alkylamino, cycloalkylamino, arylamino, acylamino, sulfonamido or alkoxycarbonyl;

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_5$  and  $R_6$  are independently hydrogen, halogen, cyano,  $R_7$ ,  $-C(O)R_7$ , or  $-S(O)_2R_7$  wherein

$R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which

$R_8$  and  $R_9$  are, independently, hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{10}$  is hydrogen, alkyl, cycloalkyl, aryl or heterocyclyl; or  $R_{10}$  and  $R_{11}$ , combined, are alkylene which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

$m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

provided that: (1)  $R_5$  and  $R_6$  are not halogen when  $n$  is zero; or (2)  $R_5$  is not  $-S(O)_2R_7$ ,

wherein  $R_7$  is  $-(CR_8R_9)_m-W-R_{10}$  in which  $m$  is zero,  $W$  is a bond and  $R_{10}$  is  $C_{1-3}$ alkyl when  $n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

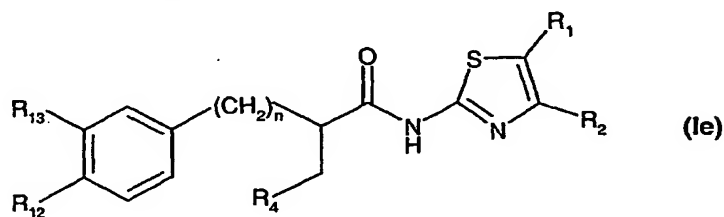
9. A compound according to Claim 8, wherein

$R_4$  is cyclopentyl;

$n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

10. A compound according to Claim 1 of the formula



wherein

$R_1$  and  $R_2$  are independently hydrogen or halogen;

$R_4$  is  $C_{2-4}$ alkyl,  $C_{3-7}$ cycloalkyl or  $C_{5-7}$ heterocycloalkyl;

$R_{12}$  and  $R_{13}$  are independently hydrogen, halogen, cyano,  $R_{14}$ ,  $-C(O)R_{14}$ , or  $-S(O)_2R_{14}$

wherein

$R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which

$R_8$  and  $R_9$  are, independently, hydrogen or lower alkyl;

$W$  is a bond, O, S or  $-NR_{11}$  in which

$R_{11}$  is hydrogen or lower alkyl;

$R_{15}$  is cycloalkyl, aryl or heterocyclyl; or  $R_{15}$  and  $R_{11}$ , combined, are alkylene

which together with the nitrogen atom to which they are attached form a 5- to 7-membered ring;

$m$  is zero or an integer from 1 to 5;

$n$  is zero or an integer of 1 or 2;

provided that: (1)  $R_{12}$  and  $R_{13}$  both are not hydrogen, halogen, cyano or combinations thereof; (2)  $R_{12}$  is not  $-S(O)_2R_{14}$  wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is a bond when  $n$  is zero; (3)  $R_{12}$  is not  $-S(O)_2R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $R_8$  and  $R_9$  are hydrogen,  $m$  is 1 and  $W$  is a bond when  $n$  is zero; (4)  $R_{12}$  is not  $R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is O when  $n$  is zero; or (5)  $R_{12}$  is not  $R_{14}$ , wherein  $R_{14}$  is  $-(CR_8R_9)_m-W-R_{15}$  in which  $m$  is zero and  $W$  is a bond when  $n$  is zero; or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.



11. A compound according to Claim 10, wherein

$R_4$  is cyclopentyl;

$n$  is zero;

or an optical isomer thereof; or a pharmaceutically acceptable salt thereof.

12. A method for the activation of glucokinase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

13. A method for the prevention and/or treatment of conditions associated with glucokinase activity in mammals which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

14. The method according to Claim 13, which method comprises administering said compound in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; PPAR ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; PTP-1B inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid or aspirin.

15. A method for the treatment of impaired glucose tolerance, Type 2 diabetes and obesity which method comprises administering to a mammal in need thereof a therapeutically effective amount of a compound of Claim 1.

16. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with one or more pharmaceutically acceptable carriers.

17. A pharmaceutical composition comprising a therapeutically effective amount of a compound of Claim 1 in combination with a therapeutically effective amount of insulin, insulin derivative or mimetic; insulin secretagogue; insulinotropic sulfonylurea receptor ligand; PPAR ligand; insulin sensitizer; biguanide; alpha-glucosidase inhibitors; GLP-1, GLP-1 analog or mimetic; DPPIV inhibitor; HMG-CoA reductase inhibitor; squalene synthase inhibitor; FXR or LXR ligand; cholestyramine; fibrates; nicotinic acid; or aspirin.

18. A pharmaceutical composition according to claim 16 or 17 for the treatment of impaired glucose tolerance, Type 2 diabetes and obesity.
19. A compound of formula 1 according to claim 1, for use as a medicament.
20. Use of a compound of formula 1 according to claim 1, for the preparation of a pharmaceutical composition for the treatment of conditions associated with glucokinase activity activity.
21. A pharmaceutical composition according to claim 16 or 17, for use as medicament.
22. Use of a pharmaceutical composition according to claim 16 or 17, for the preparation of a medicament for the treatment of conditions associated with glucokinase activity.
23. Use according to any one of claims 20 or 22 wherein the conditions associated with glucokinase activity is selected from impaired glucose tolerance, Type 2 diabetes, insulin resistance, dyslipidemia, metabolic syndrome X and obesity.

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